Epperson 09/763,308

```
=> d his 1

     (FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT
     13:14:35 ON 11 MAR 2003)
L29          53 DUP REM L28 (55 DUPLICATES REMOVED)

=> d que l29
L1          219 SEA ARVIDSSON P?/AU
L2           94 SEA DIVERS M?/AU
L3           12 SEA ("PETERSENMAHRT E"/AU OR "PETERSENMAHRT S"/AU OR "PETERSENM
                AHRT S K"/AU OR "PETERSENMARHT S"/AU)
L4           37 SEA ("PETERSEN MAHRT S"/AU OR "PETERSEN MAHRT S K"/AU OR
                "PETERSEN MAHRT SILJA"/AU OR "PETERSEN MAHRT SILJA K"/AU)
L5          360 SEA (L1 OR L2 OR L3 OR L4)
L6            6 SEA L5 AND CYCLODEXTRIN?
L7          551 SEA CYCLODEXTRIN? (5A)(STORAGE# OR PROTECT? OR PRESERV?)
L8          218 SEA L7 (5A) BETA
L9            1 SEA L8 AND LIBRAR?
L10           1 SEA L8 AND COMBINATOR?
L11           0 SEA L8 AND (PARALELL(3A) SYNTHE?)
L12           0 SEA L8 AND (HIGH(3A) THROUGHPUT)
L13          16 SEA L8 AND MM
L14          38 SEA L8 (5A) HYDROXYPROPYL
L27         103 SEA (L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR L15 OR L16 OR
                L17 OR L18 OR L19) OR (L22 OR L23 OR L24 OR L25 OR L26)
L28         108 SEA L27 OR L6
L29          53 DUP REM L28 (55 DUPLICATES REMOVED)


=> d ibib abs l29 1-53

L29  ANSWER 1 OF 53  HCAPLUS  COPYRIGHT 2003 ACS
ACCESSION NUMBER:         2002:819966  HCAPLUS
DOCUMENT NUMBER:          137:309913
TITLE:                    Food preservatives containing carbohydrates and their
                          manufacture from chitosan
INVENTOR(S):              Nakai, Yoshinaga
PATENT ASSIGNEE(S):       Japan
SOURCE:                   Jpn. Kokai Tokkyo Koho, 6 pp.
                          CODEN: JKXXAF
DOCUMENT TYPE:            Patent
LANGUAGE:                 Japanese
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     ---------------   ----  --------       ---------------  --------
     JP 2002315551      A2   20021029       JP 2001-121596   20010419
PRIORITY APPLN. INFO.:                   JP 2001-121596      20010419
AB   Food preservatives contg. carbohydrates are manufd. by producing mixed
     polysaccharides composed of amino sugars, mannuronic acid, and guluronic
     acid, converting a part of the mannuronic acid into guluronic acid with
     isomerases, and degrading the resulting 2nd mixed
     polysaccharides with catalysts.  An aq. compn. contg. skim milk, starch
     (Swely Gel 705), chitosan, citric acid, and EtOH was stirred with
     .alpha.-amylase (Amylase AD) at 45.degree. for 50 min, stirred with
     pullulanase (Debranching Enzyme) at 25.degree. for 20 min, stirred with
     .beta.-dextrin at 65.degree. for 39 min, stirred with vegetable oil at
     room temp. for 5 h, and cooled to .apprx.0.degree. to give a food
```

Search completed by David Schreiber 308-4292

preservative contg. oligosaccharides. An aq. soln. prepd. by 5000-fold diln. of the preservative inhibited the growth of bacteria in tofu.

L29 ANSWER 2 OF 53 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2002622315 IN-PROCESS
DOCUMENT NUMBER: 22267488 PubMed ID: 12379923
TITLE: **Protective** effect of sulfobutyl ether **beta-cyclodextrin** on DY-9760e-induced hemolysis in vitro.
AUTHOR: Nagase Y; Hirata M; Arima H; Tajiri S; Nishimoto Y; Hirayama F; Irie T; Uekama K
CORPORATE SOURCE: Tokyo Pharmaceutical Research Center, Pharmaceutical Technology Research Laboratories, Daiichi Pharmaceutical Company, 1-16-13, Kitakasai, Edogawa-ku, Tokyo 134-8630, Japan.
SOURCE: JOURNAL OF PHARMACEUTICAL SCIENCES, (2002 Nov) 91 (11) 2382-9.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20021017
Last Updated on STN: 20021213

AB The hemolytic behavior of a novel cytoprotective agent, DY-9760e (3-[2-[4-(3-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-5,6-dimethoxy-1-(4-imidazolylmethyl)-1H-indazole dihydrochloride 3.5 hydrate) was investigated using rabbit erythrocytes. Further, the effects of water-soluble cyclodextrin derivatives, such as 2-hydroxypropyl-beta-cyclodextrin (HP-beta-CyD) and sulfobutyl ether of beta-cyclodextrin (SBE-beta-CyD), on the hemolytic activity of DY-9760e were studied. DY-9760e induced hemolysis at concentrations >0.2-0.3 **mM** in phosphate buffered saline (PBS) of pH 4.0 and 6.0, where DY-9760e is predominantly in dicationic and monocationic forms, respectively. The hemolytic activity of the monocationic DY-9760e was higher than that of the dicationic species, and the hemolysis at pH 4.0 involved the formation of methemoglobin. DY9760e induced the morphological change of erythrocytes towards membrane invagination at both pH 4.0 and 6.0. SBE7-beta-CyD significantly suppressed the DY-9760e-induced hemolysis and morphological change at both pH 4.0 and 6.0, as well as the formation of methemoglobin at pH 4.0. On the other hand, HP-beta-CyD suppressed only the hemolysis, but neither the morphological change nor the formation of methemoglobin. In addition, the inhibitory effect of SBE7-beta-CyD on the hemolysis was greater than that of HP-beta-CyD. The superior inhibitory effect of SBE7-beta-CyD on the DY-9760-induced hemolysis, the morphological change, and the formation of methemoglobin may be attributable to the formation of a stable inclusion complex with DY-9760e and to the weaker hemolytic activity of SBE7beta-CyD than HP-beta-CyD. These results suggest potential use of SBE7-beta-CyD as a parenteral carrier for DY-9760e.

L29 ANSWER 3 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 2
ACCESSION NUMBER: 2002:664293 HCAPLUS
DOCUMENT NUMBER: 137:354607
TITLE: **Synthesis** of new cuniform molecular host model based on .beta.-cyclodextrin
AUTHOR(S): Hao, Ai-you; Wang, Jin-shan
CORPORATE SOURCE: School of Chemistry & Chemical Eng., Shandong Univ.,

Jinan, 250100, Peop. Rep. China
SOURCE: Huaxue Xuebao (2002), 60(8), 1536-1538
CODEN: HHHPA4; ISSN: 0567-7351
PUBLISHER: Kexue Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB **.beta.-Cyclodextrin** with the 6-hydroxyls **protected** by dimethyl-tert-butylsilyl was selectively oxidized by lead tetraacetate. After the silyl groups were removed by boron fluoride-etherate, mono-2,3-dialdehyde-.beta.-cyclodextrin as a cuniform mol. could be constructed. Mono-2,3-dialdehydo-.beta.-cyclodextrin is more sol. in water than .beta.-cyclodextrin. Mono-2,3-dialdehydo-.beta.-cyclodextrin could be used as the mobile phase additives for effective resoln. of DL-adrenaline on silica gel plates.

L29 ANSWER 4 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:124426 HCAPLUS
TITLE: Inclusion process of volatile oil in Naomai I capsule
AUTHOR(S): Yuan, Xiaohong; Hu, Xuejun; Liu, Maocai
CORPORATE SOURCE: Second Affiliated Hospital, Guangzhou University of TCM, Canton, 510120, Peop. Rep. China
SOURCE: Zhongguo Yiyuan Yaoxue Zazhi (2002), 22(8), 451-453
CODEN: ZYYAEP; ISSN: 1001-5213
PUBLISHER: Zhongguo Yiyuan Yaoxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB The inclusion process for volatile oil in Naomai I capsule was studied. Orthogonal expt. **design** and GC/MS anal. were used. Using utility rate of volatile oil, **collecting** rate and oil content of inclusion compds. as index, the optimal inclusion conditions for volatile oil with satd. soln. method were gained as follows: a proportion of 1:4 (ml:g) for oil to beta- cyclodextrin, stirring for 2 h at 40.degree.C. GC/MS anal. showed that the main components of volatile oil before and after being covered had no significant difference. **Beta-cyclodextrin** inclusion compd. could effectively **preserve** the active components of volatile oil and the optimal inclusion process was reliable.

L29 ANSWER 5 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:73625 HCAPLUS
TITLE: Evaluation of toxicity and antitumour effects of a hydroxypropyl .beta.-cyclodextrin inclusion complex of quercetin
AUTHOR(S): Indap, M. A.; Bhosle, Sunita C.; Tayade, P. T.; Vavia, P. R.
CORPORATE SOURCE: Chemotherapy Division, Cancer Research Institute, Mumbai, 400 012, India
SOURCE: Indian Journal of Pharmaceutical Sciences (2002), 64(4), 349-353
CODEN: IJSIDW; ISSN: 0250-474X
PUBLISHER: Indian Pharmaceutical Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The general toxicity and antineoplastic activity of a hydroxypropyl beta cyclodextrin complex were investigated recently by us. Complexed quercetin at the large LD of 400 mg/kg was not found to be toxic. (Free quercetin can be administered only at smaller doses because of its poor aq. soly.). The max. tolerated dose corresponding to the LD10 was > 400 mg/kg for hydroxypropyl beta cyclodextrin complex of quercetin obtained

after a single i.p. application which proved to be less toxic than quercetin. In vitro expts. have shown that hydroxypropyl beta cyclodextrin complex of quercetin induces apoptosis in both K-562 and B16F10 melanoma cells. Therapeutic expts. in C3H/J mice implanted with mammary adenocarcinoma cells resulted in significantly increased effectiveness of hydroxypropyl beta cyclodextrin complex of quercetin compared to free quercetin. We obsd. no apparent toxicity to bone marrow of irradiated Swiss mice previously administered hydroxypropyl beta cyclodextrin complex of quercetin for a week. This suggest that **hydroxypropyl beta cyclodextrin** complex was able to **protect** bone marrow cells from lethal effect of radiation. When the cytotoxicities of quercetin and its complexes were compared on erythrocytes of rat and rabbits, no significant differences were obsd. The ability to selectively target quercetin via its cyclodextrin inclusion complex against cancer growth could improve the therapeutic effectiveness of cyclodextrin prepns. as well as reduce adverse side effects assocd. with quercetin. The new cyclodextrin inclusion complex appears to have high potential for the treatment of leukemias and possibly also for solid tumors.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 6 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:140631 HCAPLUS
DOCUMENT NUMBER: 136:299629
TITLE: Microencapsulation protects immunoglobulin in yolk (IgY) specific against Helicobacter pylori urease
AUTHOR(S): Chang, H.-M.; Lee, Y.-C.; Chen, C. C.; Tu, Y.-Y.
CORPORATE SOURCE: Graduate Inst. of Food Science and Technology, National Taiwan Univ., Taipei, 106-17, Taiwan
SOURCE: Journal of Food Science (2002), 67(1), 15-20
CODEN: JFDSAZ; ISSN: 0022-1147
PUBLISHER: Institute of Food Technologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hens were i.m. immunized on thighs by using urease (E.C. 3.5.1.5) from H. pylori as antigen. The specificity of IgY against urease of H. pylori increased gradually after initial immunization. The **collected** yolk was microencapsulated with 10% or 20% .beta.-cyclodextrin (.beta.-CD) and gum arabic by a spray-drier. Microencapsulation was effective in protecting the IgY activity against pepsin. Liposome prepd. at the lecithin/cholesterol ratio of 1/0.25 (mole/mol) displayed satisfactory encapsulation efficiency (69%) of IgY. Increase in cholesterol content in the liposomal structure exhibited a stronger protection effect of IgY against pepsin and acid.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 7 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:152612 HCAPLUS
DOCUMENT NUMBER: 134:188174
TITLE: Use of **cyclodextrin** for protective storage of chemical **compound libraries**
INVENTOR(S): **Arvidsson, Per-Ola; Divers, Mark; Petersen-Mahrt, Silja**
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent

Search completed by David Schreiber 308-4292

Epperson 09/763,308

LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014291	A1	20010301	WO 2000-SE1592	20000821
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212270	A1	20020612	EP 2000-957180	20000821
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003507722	T2	20030225	JP 2001-518385	20000821

PRIORITY APPLN. INFO.: SE 1999-2988 A 19990824
WO 2000-SE1592 W 20000821

AB The invention relates to **cyclodextrin** as a protective agent for compds. in compd. **libraries**, particularly for use in **screening** the compd. **library** for biol. activity. A particular advantage is improved recovery of potential activity of compds. within the **library** when the compds. have dried on storage.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 8 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 3
ACCESSION NUMBER: 2001:288216 HCAPLUS
DOCUMENT NUMBER: 135:19850
TITLE: Chitosan Derivatives Bearing Pendant Cyclodextrin Cavities: **Synthesis** and Inclusion Performance
AUTHOR(S): Auzely-Velty, Rachel; Rinaudo, Marguerite
CORPORATE SOURCE: Centre de Recherches sur les Macromolecules Vegetales (CNRS) Universite Joseph Fourier de Grenoble, Grenoble, 38041, Fr.
SOURCE: Macromolecules (2001), 34(11), 3574-3580
CODEN: MAMOBX; ISSN: 0024-9297
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A new **synthetic** route to .beta.-cyclodextrin-linked chitosan was developed. This was based on the prepn. of a monosubstituted .beta.-cyclodextrin (.beta.-CD) deriv. possessing a reducing sugar on the primary face followed by its reductive amination. The CD-polysaccharide was fully characterized in terms of chem. integrity and purity by high-resoln. NMR and light scattering. The formation of inclusion complexes was investigated by NMR spectroscopy using tert-butylbenzoic acid and (+)-catechin as model guests. Inclusion properties of the grafted .beta.-CDs were shown to be similar to those of native .beta.-CD in terms of complex geometry and affinity const. These results confirm that the pendant **.beta.-cyclodextrin preserves** its conformation and its complexing characteristics.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Search completed by David Schreiber 308-4292

L29 ANSWER 9 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 4
ACCESSION NUMBER: 2001:154997 HCAPLUS
DOCUMENT NUMBER: 135:3531
TITLE: Protection of boar spermatozoa from cold shock damage by 2-hydroxypropyl-beta-cyclodextrin
AUTHOR(S): Zeng, W. X.; Terada, T.
CORPORATE SOURCE: Animal Reproduction, Faculty of Applied Biological Science, Hiroshima University, Hiroshima, 739-8528, Japan
SOURCE: Theriogenology (2001), 55(2), 615-627
CODEN: THGNBO; ISSN: 0093-691X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study examd. whether 2-hydroxypropyl-beta-cyclodextrin (HBCD) could play a role in protecting spermatozoa from cold shock, as judged by motility parameters, intact acrosomes, and membrane integrity. Motility parameters were assessed by a computer-assisted sperm motility anal. (CASA) system, and the acrosome and membrane integrity were evaluated by fluorescent staining with FITC-labeled peanut agglutinin and SYBR-14 plus Propidium Iodide, resp. The addn. of HBCD to the BF5 extender significantly increased the percentages of spermatozoa with intact acrosomes and increased membrane integrity after cold shock. The motility, progressive motility, and progressive velocity of the cold-shocked spermatozoa in the presence of HBCD were significantly higher than in the absence of HBCD. In contrast, further supplement of HBCD with cholesterol-3-sulfate (a cholesterol analog) resulted in a decrease in all the aforementioned criteria, suggesting that the ability of HBCD to protect spermatozoa from cold shock injury is blocked by satg. the cholesterol binding sites of HBCD. It is therefore concluded that HBCD protects spermatozoa against cold shock injury, possibly due to its ability to remove membrane cholesterol.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 10 OF 53 MEDLINE
ACCESSION NUMBER: 2002048410 MEDLINE
DOCUMENT NUMBER: 21632399 PubMed ID: 11775960
TITLE: Interaction of [D-Trp6, Des-Gly10] LHRH ethylamide and hydroxy propyl **beta-cyclodextrin** (HPbetaCD): thermodynamics of interaction and **protection** from **degradation** by alpha-chymotrypsin.
AUTHOR: Koushik K N; Bandi N; Kompella U B
CORPORATE SOURCE: Department of Pharmaceutical Sciences, 986025 University of Nebraska Medical Center, Omaha, NE 68198-6025, USA.
SOURCE: PHARMACEUTICAL DEVELOPMENT AND TECHNOLOGY, (2001 Nov) 6 (4) 595-606.
Journal code: 9610932. ISSN: 1083-7450.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200205
ENTRY DATE: Entered STN: 20020125
Last Updated on STN: 20020530
Entered Medline: 20020528
AB PURPOSE: The purpose of this study is to investigate the mechanisms and

thermodynamics of the interaction between hydroxypropyl beta-cyclodextrin (HPdetaCD) and [D-Trp6, des-Gly10] LHRH ethylamide (deslorelin), a **peptide** drug. METHODS: We used UV and fluorescence spectroscopy to study the interaction of HPbetaCD and deslorelin. Circular dichroism was used to study the conformational changes induced in deslorelin upon interaction with HP beta CD. The thermodynamics of the interaction of deslorelin and HPbetaCD was studied using isothermal titration calorimetry (ITC). We also determined the effect of HPbetaCD on the **degradation** of deslorelin by alpha-chymotrypsin. RESULTS: UV and fluorescence spectroscopy indicated that HPbetaD induced a change in polarity of the environment surrounding the chromophores of deslorelin. Wavelength selective fluorescence indicated an increase in the fluorescence polarization of deslorelin with an increase in excitation wavelength in the presence of HPbetaCD suggesting that tryptophan is present in a media of reduced mobility. Circular dichroism studies indicated that HPbetaCD stabilizes the conformation of deslorelin. In addition, ITC indicated an exothermic reaction between deslorelin and HPbetaCD with a low enthalpy of binding of approximately -600 cal/mol and a binding affinity of approximately -1.25 x 10(2) M-1. Finally, the rate of **degradation** of deslorelin by alpha-chymotrypsin was decreased by 33% in the presence of HPbetaCD. CONCLUSIONS: These results indicate that there is an interaction between HPbetaCD and deslorelin, which involves the inclusion of aromatic amino acids of deslorelin into the hydrophobic cavity of the cyclodextrin. This inclusion, providing steric hindrance, may be one of the mechanisms by which HPbetaCD reduces enzymatic hydrolysis of deslorelin.

L29 ANSWER 11 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:590488 HCAPLUS
DOCUMENT NUMBER: 135:305169
TITLE: Stability of color pigments of paprika (Capsicum annum) powders by multiwavelength spectrometry and HPLC
AUTHOR(S): Cserhati, Tibor; Forgacs, Esther; Morais, Maria Helena; Mota, Teresa; Ramos, Ana Cristina
CORPORATE SOURCE: Institute of Chemistry, Chemical Research Center, Hungarian Academy of Sciences, Budapest, 1525, Hung.
SOURCE: Chemia Analityczna (Warsaw, Poland) (2001), 46(3), 361-368
CODEN: CANWAJ; ISSN: 0009-2223
PUBLISHER: Institute of Physical Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Multiwavelength spectrometry and reversed-phase high-performance liq. chromatog. were simultaneously used for the assessment of the effect of reduced glutathion (GLT) and hydroxypropyl-.beta.-cyclodextrin (HP-.beta.-CD) on the decompn. rate of the color pigments of paprika (Capsicum annum) powders during storage. The evaluation of the spectral and chromatog. data by principal component anal. proved that the storage time exerts the highest impact on the stability of pigments. The decompn. rate of some pigment fractions was modified in the presence of the additives, however, the effect was of secondary importance. It was found that multi-wavelength spectrometry combined with HPLC can be successfully used for the study of the stability of color pigments of paprika powder.
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 12 OF 53 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001088792 EMBASE

Search completed by David Schreiber 308-4292

TITLE: Preparation of polycyclodextrin hollow spheres by templating gold nanoparticles.
AUTHOR: Sun L.; Crooks R.M.; Chechik V.
CORPORATE SOURCE: V. Chechik, Department of Chemistry, University of York, Heslington, York YO10 5DD, United Kingdom. vc4@york.ac.uk
SOURCE: Chemical Communications, (21 Feb 2001) 7/4 (359-360). Refs: 16
ISSN: 1359-7345 CODEN: CHCOFS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Oxidation of gold nanoparticles **protected** by thiolated . **beta.-cyclodextrin** molecules, leads to formation of water-soluble polycyclodextrin nanocapsules held together by S-S bonds.

L29 ANSWER 13 OF 53 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 2001225155 MEDLINE
DOCUMENT NUMBER: 21095579 PubMed ID: 11164769
TITLE: In vivo, the direct and seizure-induced neuronal cytotoxicity of kainate and AMPA is modified by the non-competitive antagonist, GYKI 52466.
AUTHOR: Lees G J; Leong W
CORPORATE SOURCE: Departments of Psychiatry and Behavioural Science, School of Medicine, University of Auckland, Auckland, New Zealand.. gj.lees@auckland.ac.nz
SOURCE: BRAIN RESEARCH, (2001 Jan 26) 890 (1) 66-77.
Journal code: 0045503. ISSN: 0006-8993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200104
ENTRY DATE: Entered STN: 20010502
Last Updated on STN: 20010502
Entered Medline: 20010426
AB The 2,3-benzodiazepine GYKI 52466, administered intracerebrally or systemically, was assessed for its ability to protect against the neuronal death in the brain caused by intra-hippocampal injections of the non-N-methyl-D-aspartate (NMDA) receptor agonists, kainate and L-alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA). In contrast to a previous report, a low intra-hippocampal dose of GYKI 52466 (25 nmol) did not protect against kainate toxicity. In order to achieve higher doses of GYKI 52466, solubilization in 2-**hydroxypropyl-beta-cyclodextrin** was used, and limited **protection** against AMPA, but not kainate toxicity was found. There was a commensurate reduction in seizure-related neuronal loss in the limbic regions of the brain. When diazepam was used to prevent seizures, GYKI 52466 had no effect on hippocampal neuronal loss caused by the direct toxicity of AMPA and kainate on hippocampal neurons. Systemic administration of GYKI 52466 had only a minimal effect on preventing neuronal death caused by AMPA. In vivo, GYKI 52466 is only weakly effective as a neuroprotective agent.

L29 ANSWER 14 OF 53 MEDLINE DUPLICATE 6
ACCESSION NUMBER: 2001276568 MEDLINE
DOCUMENT NUMBER: 21261341 PubMed ID: 11368512
TITLE: Maintenance of quaternary structure in the frozen state stabilizes lactate dehydrogenase during freeze-drying.

Search completed by David Schreiber 308-4292

Epperson 09/763,308

AUTHOR: Anchordoquy T J; Izutsu K I; Randolph T W; Carpenter J F
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Colorado Health Sciences Center, Denver, Colorado, 80262, USA.
SOURCE: ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, (2001 Jun 1) 390 (1) 35-41.
Journal code: 0372430. ISSN: 0003-9861.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB Sugars inhibit **protein** unfolding during the drying step of lyophilization by replacing hydrogen bonds to the **protein** lost upon removal of water. In many cases, polymers fail to inhibit dehydration-induced damage to **proteins** because steric hindrance prevents effective hydrogen bonding of the polymer to the **protein** 's surface. However, in certain cases, polymers have been shown to stabilize multimeric enzymes during lyophilization. Here we test the hypothesis that this protection is due to inhibition of dissociation into subunits during freezing. To test this hypothesis, as a model system we used **mixtures** of lactate dehydrogenase isozymes that form electrophoretically distinguishable hybrid tetramers during reversible dissociation. We examined hybridization and recovery of catalytic activity during freeze-thawing and freeze-drying in the presence of polymers (dextran, Ficoll, and polyethylene glycol), sugars (sucrose, trehalose, glucose), and surfactants (Tween 80, Brij 35, hydroxy-propyl **beta -cyclodextrin**). The surfactants did not **protect** LDH during freeze-thawing or freeze-drying. Rather, in the presence of Brij 35, enhanced damage was seen during both freeze-thawing and freeze-drying, and the presence of Tween 80 exacerbated loss of active **protein** during freeze-drying. Polymers and sugars prevented dissociation of LDH during the freezing step of lyophilization, resulting in greater recovery of enzyme activity after lyophilization and rehydration. This beneficial effect was observed even in systems that do not form glassy solids during freezing and drying. We suggest that stabilization during drying results in part from greater inherent stability of the assembled holoenzyme relative to that of the dissociated monomers. Polymers inhibit freezing-induced dissociation thermodynamically because they are preferentially excluded from the surface of **proteins**, which increases the free energy of dissociation and denaturation.

L29 ANSWER 15 OF 53 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001053855 EMBASE
TITLE: Cyclodextrin solubilization of benzodiazepines: Formulation of midazolam nasal spray.
AUTHOR: Loftsson T.; Guomundsdottir H.; Sigurjonsdottir J.F.; Sigurosson H.H.; Sigfusson S.D.; Masson M.; Stefansson E.
CORPORATE SOURCE: T. Loftsson, Faculty of Pharmacy, University of Iceland, P.O. Box 7210, IS-127 Reykjavik, Iceland. thorstlo@hi.is
SOURCE: International Journal of Pharmaceutics, (5 Jan 2001) 212/1 (29-40).
Refs: 27
ISSN: 0378-5173 CODEN: IJPHDE
PUBLISHER IDENT.: S 0378-5173(00)00580-9

Search completed by David Schreiber 308-4292

Epperson 09/763,308

COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The cyclodextrin solubilization of three benzodiazepines, i.e. alprazolam, midazolam and triazolam, was investigated. The cyclodextrin solubilization was enhanced through ring-opening of the benzodiazepine rings and ionization of the ring-open forms. Additional enhancement was obtained through interaction of a water-soluble polymer with the cyclodextrin complexes. The ring-opening was pH-dependent and completely reversible, the ring-open forms dominating at low pH but the ring-closed forms at physiologic pH. The ring-closed forms were rapidly regenerated upon elevation of pH. In freshly **collected** human serum in vitro at 37.degree.C, the half-life for the first-order rate constant for the ring-closing reaction was estimated to be less than 2 min for both alprazolam and midazolam. Midazolam (17 mg/ml) was solubilized in aqueous pH 4.3 nasal formulation containing 14% (w/v) sulfobutylether . **beta.-cyclodextrin**, 0.1% (w/v) **hydroxypropyl** methylcellulose, **preservatives** and buffer salts. Six healthy volunteers received 0.06 mg/kg midazolam intranasally and 2 mg intravenously, and blood samples were **collected** up to 360 min after the administration. Midazolam was absorbed rapidly reaching maximum serum concentrations of 54.3 .+-. 5.0 ng/ml at 15 .+-. 2 min. The elimination half-life of midazolam was 2.2 .+-. 0.3 h and the absolute availability was 73 .+-. 7%. All mean values .+-. SEM. .COPYRGT. 2001 Elsevier Science B.V.

L29 ANSWER 16 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 7
ACCESSION NUMBER: 2000:396952 HCAPLUS
DOCUMENT NUMBER: 133:164418
TITLE: Dendrimers Functionalized with a Single Fluorescent Dansyl Group Attached "Off Center": **Synthesis** and Photophysical Studies
AUTHOR(S): Cardona, Claudia M.; Alvarez, Julio; Kaifer, Angel E.; McCarley, Tracy Donovan; Pandey, Siddharth; Baker, Gary A.; Bonzagni, Neil J.; Bright, Frank V.
CORPORATE SOURCE: Center for Supramolecular Science and Department of Chemistry, University of Miami, Coral Gables, FL, 33124-0431, USA
SOURCE: Journal of the American Chemical Society (2000), 122(26), 6139-6144
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of three new fluorescent dendrimers contg. a single, focally located dansyl group and 3 (1), 9 (2), and 27 (3) carboxylic acid groups in their peripheries were **synthesized** and characterized. The photophys. properties of these dendrimers were investigated in aq. soln. The host-guest interactions of the dendrimers through their dansyl subunits with .beta.-cyclodextrin and polyclonal anti-dansyl antibodies were also investigated by various methods. Photophys. measurements on the dendrimers demonstrate that the dansyl residue is progressively shielded from the solvent as the dendrimer generation increases, resulting in marked changes in spectral features, fluorescence quantum yields, excited-state fluorescence lifetimes, radiative and nonradiative decay

rates, and rotational reorientation times. The excited-state intensity decay kinetics for 1-3 are well described by a single exponential. Contrary to the popularly held belief that lower generation dendrimers are "floppy" species in soln., the mol. motions of 1-3 are described by a single rotational reorientation time. Access to the dansyl moiety is impeded with increasing dendrimer size as the dendrimer mass affords a significant degree of **protection** from binding by nonselective (. **beta.-cyclodextrin** (.**beta**.-CD)) and selective (anti-dansyl antibody) hosts for the dansyl residue. The equil. const. for .beta.-CD binding of the dansyl residue in 1 is .apprx.2.5-fold lower than that for binding to dansylamine (DA). Dendrimers 2 and 3 do not assoc. with .beta.-CD at all. Anti-dansyl antibodies can bind to the dansyl residue in dendrimers 1-3 with remarkably large binding affinities. The equil. const. for the antibody complex decreases systematically from 5.0 .times. 107 M-1 for DA to 1.5 .times. 106 M-1 for 3.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 17 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:250710 HCAPLUS
DOCUMENT NUMBER: 135:3534
TITLE: Freezability of boar spermatozoa is improved by exposure to 2-hydroxypropyl-beta-cyclodextrin
AUTHOR(S): Zeng, WenXian; Terada, Takato
CORPORATE SOURCE: Animal Reproduction, Faculty of Applied Biological Science, Hiroshima University, Higashi-Hiroshima, 739-8528, Japan
SOURCE: Reproduction, Fertility and Development (2000), 12(3,4), 223-228
CODEN: RFDEEH; ISSN: 1031-3613
PUBLISHER: CSIRO Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The influence of 2-hydroxypropyl-beta-cyclodextrin (HBCD) exposure on post-thaw spermatozoa prior to freezing using acrosome integrity and the parameters of motility was studied. Acrosomal status was monitored by means of FITC-labeled peanut agglutinin, and the motility parameters were assessed using a computer-assisted sperm motility anal. (CASA) system. The spermatozoa were exposed to HBCD over a period of 3 h, during which the cells were slowly cooled from 25 to 5.degree.C, and then frozen into pellets. The percentage of frozen-thawed spermatozoa with intact acrosomes in 40 **mM** HBCD group was approx. three-fold higher than that of the control. The motility and progressive motility values of the frozen-thawed spermatozoa were found to increase significantly with increased HBCD concns. On the other hand, further addn. of cholesterol-3-sulfate to the BF5 extender contg. 20 **mM** HBCD resulted in a drastic decrease in the percentage of spermatozoa with intact acrosomes, and decreased motility and progressive motility, suggesting that cholesterol-sulfate probably counteracted the protective action of HBCD. In conclusion, the results of the present study indicate that HBCD protected boar spermatozoa against freeze-thaw damage, possibly by means of stimulating the efflux of membrane cholesterol.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 18 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:569998 HCAPLUS
DOCUMENT NUMBER: 131:322898
TITLE: **Synthesis** of characteristic palmitoylated

lipopeptides from human Y1 receptor by a combination of enzyme-labile and Pd(0)-sensitive protecting groups
AUTHOR(S): Kuhn, Karsten; Waldmann, Herbert
CORPORATE SOURCE: Max-Planck.Institut fur molekulare Physiologie, Dortmund, D-44227, Germany
SOURCE: Tetrahedron Letters (1999), 40(35), 6369-6372
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Base-labile palmitoylated **peptides** representing the characteristic lipidated region of human Y1 receptor were **synthesized**. The key steps in the chemoenzymic protecting group strategy were enzyme catalyzed cleavage of the choline ester and Pd(0)-mediated removal of the allyl ester.
REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 19 OF 53 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 1999:630308 SCISEARCH
THE GENUINE ARTICLE: 224VQ
TITLE: Multifunctional hydrophilic polymers
AUTHOR: Chiellini E (Reprint); Bizzarri R; Bonaguidi P; Talamelli P; Solaro R
CORPORATE SOURCE: UNIV PISA, DEPT CHEM & IND CHEM, VIA RISORGIMENTO 35, I-56126 PISA, ITALY (Reprint)
COUNTRY OF AUTHOR: ITALY
SOURCE: JOURNAL OF MACROMOLECULAR SCIENCE-PURE AND APPLIED CHEMISTRY, (AUG 1999) Vol. A36, No. 7-8, pp. 901-915.
Publisher: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016.
ISSN: 1060-1325.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 27
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Different types of multifunctional hydrophilic polymers were **synthesized** and characterized in view of their possible biomedical application. Several poly(amide)s and poly(ester-amide)s containing oligo(oxyethylene) segments and tartaric or succinic acid residues were prepared by activated polycondensation methods. New functional derivatives of beta-cyclodextrin were obtained by reaction with glycidyl ether of **protected** polyols. The mechanism of **beta-cyclodextrin** polymerization with epichlorohydrine was investigated by C-13-NMR spectroscopy.

L29 ANSWER 20 OF 53 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 2000042882 MEDLINE
DOCUMENT NUMBER: 20042882 PubMed ID: 10575628
TITLE: Protective colloids and polylactic acid co-affecting the polymorphic crystal forms and crystallinity of indomethacin encapsulated in microspheres.
AUTHOR: Lin S Y; Chen K S; Teng H H
CORPORATE SOURCE: Department of Medical Research and Education, Veterans General Hospital-Taipe, Shih-Pai, Taipei, Taiwan, ROC.. sylin@vghtpe.gov.tw
SOURCE: JOURNAL OF MICROENCAPSULATION, (1999 Nov-Dec) 16 (6) 769-76.

Search completed by David Schreiber 308-4292

Journal code: 8500513. ISSN: 0265-2048.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000204
Last Updated on STN: 20000204
Entered Medline: 20000124

AB The co-effect of protective colloids and polylactic acid (PLA) on the polymorphic crystal forms and crystallinity of indomethacin (IMC) in IMC-loaded PLA microspheres was investigated with differential scanning calorimetry, infrared spectroscopy and x-ray diffractometry, to evaluate the polymorphic crystal forms and crystallinity of IMC encapsulated in PLA microspheres. The surfactant, sodium dodecyl sulphate (SDS), was also used as a dispersing agent. The results indicate that the polymorphism and crystallinity of IMC encapsulated in IMC-loaded PLA microspheres was dependent on the type of protective colloid and PLA used. The amorphous state and alpha-form of IMC were found in the IMC-loaded PLA microspheres prepared using polysaccharide (pectin or **beta-cyclodextrin**) as a **protective** colloid or SDS as a dispersing agent. However, the amorphous and methylene chloride solvate of IMC seemed to exist in the IMC-loaded PLA microspheres prepared with the **proteins** (gelatin or albumin), **synthetic** cellulose derivative (methyl cellulose or hydroxylpropyl methylcellulose) or the **synthetic** nonionic polymer (polyvinyl alcohol, polyvinyl pyrrolidone or biosoluble polymer) as a protective colloid. PLA was found to express a certain crystallinity in microspheres and not be affected by the protective colloids, but it played a more important role in influencing the crystallization of IMC during microencapsulation than the protective colloids. No interaction occurred in the physical **mixture** of IMC and PLA, nor in the IMC-loaded PLA microspheres.

L29 ANSWER 21 OF 53 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 2000071955 MEDLINE
DOCUMENT NUMBER: 20071955 PubMed ID: 10605939
TITLE: Cholesterol does not affect the toxicity of amyloid beta fragment but mimics its effect on MTT formazan exocytosis in cultured rat hippocampal neurons.
AUTHOR: Abe K; Saito H
CORPORATE SOURCE: Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, The University of Tokyo, Japan.. kazuhoab@mol.f.u-tokyo.ac.jp
SOURCE: NEUROSCIENCE RESEARCH, (1999 Dec 1) 35 (3) 165-74.
Journal code: 8500749. ISSN: 0168-0102.
PUB. COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000112

AB It has recently been reported that methyl-**beta-cyclodextrin**-solubilized cholesterol **protects** PC12 cells from amyloid **beta protein** (Abeta) toxicity. To ask if this is the case in brain neurons, we investigated its effect in primary cultured rat hippocampal neurons. In basal culture conditions with no addition of Abeta, methyl-beta-cyclodextrin-solubilized cholesterol at

concentrations of 30-100 microM was toxic to neurons, but at concentrations of 1-10 microM promoted neuronal survival. Methyl-beta-cyclodextrin-solubilized cholesterol at 1-10 microM was also effective in protecting neurons from toxicity of 20 microM Abeta. However, these effects were all mimicked by methyl-beta-cyclodextrin alone, but not by cholesterol solubilized by dimethylsulfoxide or ethanol. The effects of methyl-beta-cyclodextrin-solubilized cholesterol on neuronal survival and Abeta toxicity are probably attributed to the action of methyl-beta-cyclodextrin, but not cholesterol. Alternatively, we found that methyl-beta-cyclodextrin-solubilized cholesterol at lower concentrations (> 10 nM) inhibited cellular reduction of 3-(4,5-dimethylthiazol-2-yl)-2.5-diphenyltetrazolium bromide (MTT) by promoting the exocytosis of MTT formazan. This effect was shared by dimethylsulfoxide- or ethanol-solubilized cholesterol, but not by methyl-beta-cyclodextrin, supporting that it is attributed to the action of cholesterol. These results suggest that cholesterol does not protect neurons from Abeta toxicity, or rather inhibits cellular MTT reduction in a similar manner to Abeta.

L29 ANSWER 22 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:137998 HCAPLUS
DOCUMENT NUMBER: 130:209888
TITLE: A convenient **synthesis** of per-O-methylated 6-O-monosubstituted .beta.-cyclodextrins
AUTHOR(S): Lupescu, Niculina; Ho, Catherine K. Y.; Jia, Guochen; Krepinsky, Jiri J.
CORPORATE SOURCE: Department of Medical Genetics and Microbiology, and Protein Engineering Network of Centers of Excellence, University of Toronto, Toronto, ON, M5S 1A8, Can.
SOURCE: Journal of Carbohydrate Chemistry (1999), 18(1), 99-104
CODEN: JCACDM; ISSN: 0732-8303
PUBLISHER: Marcel Dekker, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 130:209888
AB Title per-O-methylated 6-O-monosubstituted **.beta.-cyclodextrins** were prepd. using triflate as **protective** group for nucleophilic substitution.
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 23 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:234396 HCAPLUS
DOCUMENT NUMBER: 136:42678
TITLE: Validation of animal experiments on ciliary function in vitro. II. The influence of absorption enhancers, preservatives and physiologic saline
AUTHOR(S): Boek, Wilbert M.; Romeijn, Stefan G.; Graamans, Kees; Verhoef, J. Coos; Merkus, Frans W. H. M.; Huizing, Egbert H.
CORPORATE SOURCE: Department of Otorhinolaryngology, University Hospital Utrecht, Utrecht, Neth.
SOURCE: Acta Oto-Laryngologica (1999), 119(1), 98-101
CODEN: AOLAAJ; ISSN: 0001-6489
PUBLISHER: Scandinavian University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ciliary beat frequency (CBF) is one of the most important parameters of

mucociliary clearance. Previously, we demonstrated that mucosa from chicken embryo trachea is a good substitute for human ciliated epithelium to study the effects on CBF of substances that are used clin. In this study, we examd. the effect on CBF of four excipients for nasal drug formulations: the absorption enhancers methylated .beta.-cyclodextrin 2% and sodium taurodihydrofusidate 1%, the preservative benzalkonium chloride 0.01%, and physiol. saline. We also examd. the effect on CBF of the cryopreservative DMSO, which is used to protect ciliated epithelium prior to storage in liq. nitrogen. Results obtained with chicken embryo trachea were compared with those of cryopreserved human mucosa taken from the sphenoidal sinus. For all of the substances tested, the effects on CBF of chicken material were comparable to those measured on human material. Benzalkonium chloride had a stronger ciliostatic effect on human tissue. After 60 min, however, the effect of that substance on CBF was similar in both tissues. We conclude that chicken embryo trachea can be used as a substitute for human ciliated mucosa when studying ciliary activity in vitro.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 24 OF 53 MEDLINE DUPLICATE 10
ACCESSION NUMBER: 1999174885 MEDLINE
DOCUMENT NUMBER: 99174885 PubMed ID: 10077267
TITLE: Metachromatic activity of beta-cyclodextrin sulfates as heparin mimics.
AUTHOR: Baumann R; Rys P
CORPORATE SOURCE: Laboratorium fur Technische Chemie, Eidgenossische Tecnische Hochschule Zurich, Switzerland.
SOURCE: INTERNATIONAL JOURNAL OF BIOLOGICAL MACROMOLECULES, (1999 Jan) 24 (1) 15-8.
Journal code: 7909578. ISSN: 0141-8130.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 19990607
Last Updated on STN: 19990607
Entered Medline: 19990521

AB Heparin is a versatile biologically active substance which has been reported to have an inhibitory effect on angiogenesis if administered together with hydrocortisone. Since very little is known about the mechanism of this activity, beta-cyclodextrin sulfates were prepared to mimic heparin. The sulfate groups were introduced into **beta-cyclodextrin** regioselectively using **protecting** groups.
The obtained polyanions were tested for their complex binding properties by mixing them with cationic dyes and measuring the metachromatic response which proved to be a very useful tool to evaluate the biological activity of these **compounds**. The results reveal that the activity depends largely upon the charge density at the surface of the beta-cyclodextrin sulfates: a large number of sulfate groups or anionic groups relatively close to each other display high activity, whereas molecules with fewer sulfate groups or with them more distant from each other exhibit smaller activities.

L29 ANSWER 25 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:123993 HCAPLUS
DOCUMENT NUMBER: 128:196672
TITLE: Preservative systems for pharmaceutical compositions

containing cyclodextrins
INVENTOR(S): Castillo, Ernesto J.; Espino, Ramon L.
PATENT ASSIGNEE(S): Alcon Laboratories, Inc., USA; Castillo, Ernesto J.; Espino, Ramon L.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806381	A1	19980219	WO 1997-US14119	19970808
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2232435	AA	19980219	CA 1997-2232435	19970808
AU 9739140	A1	19980306	AU 1997-39140	19970808
AU 709580	B2	19990902		
EP 877600	A1	19981118	EP 1997-936482	19970808
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11513045	T2	19991109	JP 1997-509954	19970808
US 5985310	A	19991116	US 1998-29943	19980310

PRIORITY APPLN. INFO.: US 1996-22453P P 19960809
WO 1997-US14119 W 19970808
OTHER SOURCE(S): MARPAT 128:196672

AB Disclosed are preservative systems useful in aq. pharmaceutical compns. contg. an active agent and a cyclodextrin. The preservative systems comprise boric acid and one or more compds. selected from the group consisting of C16 benzalkonium halide compds., polymeric quaternary ammonium compds., and quaternary ammonium alkylene glycol phospholipid derivs. [R1C(O)XR2N+(R3)(R4)Y-CH(OH)CH2O]aP(O)(OH)b (a + b = 3; R1 = C8-22 alkyl or alkene; X = NH, O, CH2; R2 = C2-6 alkyl; each R3 is independently C1-12 alkyl or alkene; and Y is nothing or C1-6 alkyl or alkene) and pharmaceutically acceptable salts thereof. A pharmaceutical formulation contained betaxolol.HCl 0.56, hydroxypropyl .beta.-cyclodextrin 7.5, boric acid 0.5, sodium chloride 0.3, EDTA 0.01, benzalkonium chloride 0.015, NaOH/HCl q.s. pH = 6.6, and water q.s. 100%. Antimicrobial preservative effectiveness of the compn. was tested on bacteria and fungi.

L29 ANSWER 26 OF 53 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 1998:818847 SCISEARCH
THE GENUINE ARTICLE: 130TR
TITLE: Regioselective alkylation of beta-cyclodextrin
AUTHOR: Bansal P S; Francis C L (Reprint); Hart N K; Henderson S A; Oakenfull D; Robertson A D; Simpson G W
CORPORATE SOURCE: CSIRO MOL SCI, PRIVATE BAG 10, CLAYTON S MDC, CLAYTON, VIC 3169, AUSTRALIA (Reprint); FOOD SCI AUSTRALIA, N RYDE, NSW 2113, AUSTRALIA; CSIRO MOL SCI, CLAYTON, VIC 3169, AUSTRALIA; AMRAD OPERAT PTY LTD, RICHMOND, VIC 3121, AUSTRALIA
COUNTRY OF AUTHOR: AUSTRALIA
SOURCE: AUSTRALIAN JOURNAL OF CHEMISTRY, (OCT 1998) Vol. 51, No. 10, pp. 915-923.
Publisher: C S I R O PUBLICATIONS, 150 OXFORD ST, PO BOX 1139, COLLINGWOOD VICTORIA 3066, AUSTRALIA.
ISSN: 0004-9425.
DOCUMENT TYPE: Article; Journal

FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 25

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Methodology for preparation of heptakis(2,6-di-O-alkyl)-beta-cyclodextrins, heptakis(2-O-alkyl)-beta-cyclodextrins, and heptakis(6-O-alkyl)-beta-cyclodextrins in substantially purified form has been developed. Treatment of beta-cyclodextrin (1) with sodium or barium hydroxide and various alkyl halides in dimethyl sulfoxide or a mixture of dimethyl sulfoxide and N,N-dimethylformamide provided the corresponding heptakis(2,6-di-O-alkyl)-beta-cyclodextrins. Treatment of heptakis(6-O-t-butyldimethylsilyl)beta-cyclodextrin (5) with sodium hydroxide and several haloalkanes in dimethyl sulfoxide followed by desilylation provided heptakis(2-O-alkyl)-**beta-cyclodextrins**. **Protection** of the secondary hydroxy groups of the t-butyldimethylsilyl-beta-cyclodextrin (5) as benzyl ethers, followed by desilylation, alkylation, and debenzylation afforded several heptakis(6-O-alkyl)-beta-cyclodextrins. Analytical methodology has been developed to characterize all of these **compounds**, with the homogeneity of the pattern of substitution verified by h.p.l.c. analysis, f.a.b.-mass spectrometry and n.m.r, spectroscopy.

L29 ANSWER 27 OF 53 MEDLINE DUPLICATE 11
ACCESSION NUMBER: 1999079060 MEDLINE
DOCUMENT NUMBER: 99079060 PubMed ID: 9862067
TITLE: Development of a toxin-binding agent as a treatment for tunicaminyluracil toxicity: protection against tunicamycin poisoning of sheep.
AUTHOR: May C; Stewart P L
CORPORATE SOURCE: Plant Toxins Unit, CSIRO Australian Animal Health Laboratory, Geelong, Victoria.
SOURCE: AUSTRALIAN VETERINARY JOURNAL, (1998 Nov) 76 (11) 752-6. Journal code: 0370616. ISSN: 0005-0423.
PUB. COUNTRY: Australia
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990504
Last Updated on STN: 19990504
Entered Medline: 19990421

AB OBJECTIVE: To assess the ability of certain derivatives of beta-cyclodextrin to treat sheep affected by tunicaminyluracil toxicity, using tunicamycin poisoning as a model system. **DESIGN**: Controlled treatment trial. ANIMALS: One hundred and sixty Merino wethers were used in the studies. PROCEDURE: Groups of sheep were experimentally poisoned with tunicamycin. Derivatives of beta-cyclodextrin, with or without magnesium sulphate and magnesium gluconate, were administered to treatment groups daily for 2 to 3 days. Treatment groups were compared with untreated groups in terms of survival. RESULTS: A significant increase in survival was observed following treatment of tunicamycin-affected sheep with hydroxypropyl-beta-cyclodextrin (HP beta-CD) and magnesium sulphate in solution ($P < 0.05$). In subsequent trials, formulation of the cyclodextrin in the form of a magnesium gluconate gel suspension demonstrated significant protection ($P < 0.01$) and was equally as effective as the cyclodextrin in solution, but required half the frequency of administration, even when the treatment was not commenced until 24 h after the final toxin dose. Beta-cyclodextrin-epichlorohydrin copolymer also improved the survival rate. After toxin

administration, the sheep lost significantly less weight if treatment with HP beta-CD was commenced early ($P < 0.001$). CONCLUSION: **Protection** studies using these two **beta-cyclodextrin** derivatives suggest that they may be effective in increasing the survival of sheep poisoned by tunicamycin and warrant further testing in field outbreaks of annual ryegrass toxicity.

L29 ANSWER 28 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1998:297273 HCAPLUS
DOCUMENT NUMBER: 129:19582
TITLE: Functionality of protective colloids affecting the formation, size uniformity and morphology of drug-free polylactic acid microspheres
AUTHOR(S): Lin, S. -Y.; Chen, K. -S.; Teng, H. -H.
CORPORATE SOURCE: Department of Medical Research and Education, Veterans General Hospital, Taipei, Taiwan
SOURCE: Journal of Microencapsulation (1998), 15(3), 383-390
CODEN: JOMIEF; ISSN: 0265-2048
PUBLISHER: Taylor & Francis Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Drug-free polylactic acid (PLA) microspheres were prepd. by an emulsification-solvent evapn. technique using different types of protective colloids. The influence of 5 types of hydrophilic polymers (polysaccharides, **proteins**, **synthetic** cellulose derivs., **synthetic** nonionic polymers and surfactants) on the formation, size uniformity and morphol. of PLA microspheres was investigated. Four characteristic functions (surface activity, viscosity, elec. charge and interfacial film formation) of the hydrophilic polymer aq. solns. were used to evaluate the efficacy of these protective colloids used. The results indicate that these four functions were the key parameters to achieve the formation of PLA microspheres. The best protective colloid should have high surface activity, optimum viscosity, adequate elec. charge, and form an interfacial film to give a higher recovery, better size uniformity and smoother topog. of the PLA microspheres.
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L29 ANSWER 29 OF 53 MEDLINE DUPLICATE 12
ACCESSION NUMBER: 1998023411 MEDLINE
DOCUMENT NUMBER: 98023411 PubMed ID: 9358553
TITLE: **Protection** afforded by maltosyl-**beta-cyclodextrin** against alpha-chymotrypsin-catalyzed hydrolysis of a luteinizing hormone-releasing hormone agonist, buserelin acetate.
AUTHOR: Matsubara K; Ando Y; Irie T; Uekama K
CORPORATE SOURCE: Pharma Research Laboratories, Hoechist Japan Ltd., Saitama, Japan.
SOURCE: PHARMACEUTICAL RESEARCH, (1997 Oct) 14 (10) 1401-5.
Journal code: 8406521. ISSN: 0724-8741.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980130
Last Updated on STN: 19980130
Entered Medline: 19980122

Search completed by David Schreiber 308-4292

AB PURPOSE: The present study addresses how maltosyl-beta-cyclodextrin (G2-beta-CyD) impacts upon the alpha-chymotrypsin-catalyzed hydrolysis of buserelin acetate, an agonist of luteinizing hormone-releasing hormone with emphasis upon the direct effect of G2-beta-CyD on the activity of the protease. METHODS: Kinetic and solubility studies were performed in isotonic phosphate buffer (pH 7.4) at 25 degrees C and 37 degrees C. The interaction of alpha-chymotrypsin with G2-beta-CyD in the buffer solution was examined by differential scanning calorimetry. RESULTS: G2-beta-CyD decelerated the alpha-chymotrypsin-catalyzed hydrolysis of buserelin acetate to give the 1-3 tripeptide and the 4-9 hexapeptide fragments. This deceleration can be explained solely by a non-productive encounter between a complex of the substrate with G2-beta-CyD and the protease at relatively low CyD concentrations, while the direct inhibitory effect of G2-beta-CyD on the proteolytic activity made a considerable contribution to the overall deceleration of the hydrolysis at higher CyD concentrations. Calorimetric studies indicate the presence of intermediate states in the thermal unfolding of alpha-chymotrypsin, simultaneously accompanied by the autolysis. By contrast, a two-state thermal unfolding of alpha-chymotrypsin was observed in the presence of G2-beta-CyD, suggesting reduced proteolytic activity upon binding to G2-beta-CyD. CONCLUSIONS: These results suggest that G2-beta-CyD at higher concentrations inhibits the proteolytic action of alpha-chymotrypsin through direct interaction with the protease, as well as through the formation of a non-productive complex with the substrate.

L29 ANSWER 30 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 13
ACCESSION NUMBER: 1997:259192 HCAPLUS
DOCUMENT NUMBER: 126:342625
TITLE: Determination of preservatives in food products by cyclodextrin-modified capillary electrophoresis with multiwavelength detection
AUTHOR(S): Kuo, Kuang-Lung; Hsieh, You-Zung
CORPORATE SOURCE: Department of Applied Chemistry, National Chiao Tung University, Hsinchu, Taiwan
SOURCE: Journal of Chromatography, A (1997), 768(2), 334-341
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A high-performance capillary electrophoretic method with multiwavelength detection was developed to analyze frequently used preservatives. The effects of .alpha.-cyclodextrin and **.beta.-cyclodextrin** on migration behaviors of nine **preservatives** were investigated. The preservatives were successfully sepd. within 9 min using a borax-NaOH buffer (pH 10.0) modified with 2 **mM** .alpha.-cyclodextrin. In optimized sepn. conditions, the reproducibilities of the migration times of the preservatives were satisfactory (R.S.D. values <0.99). The correlation coeffs. of the linear calibration graphs for the preservatives, ranging between 5 and 500 .mu.g ml-1, exceeded 0.991. By employing this reliable capillary electrophoresis method, preservatives in three different food products were detd.

L29 ANSWER 31 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:137440 HCAPLUS
DOCUMENT NUMBER: 126:233429
TITLE: Hypocholesterolemic action of .beta.-cyclodextrin and its effects on cholesterol metabolism in pigs fed a cholesterol-enriched diet
AUTHOR(S): Ferezou, Jacqueline; Riottot, Michel; Serougne,

Colette; Cohen-Solal, Corinne; Catala, Isabelle; Alquier, Christian; Parquet, Michel; Juste, Catherine; Lafont, Huguette; et al.
CORPORATE SOURCE: Laboratoire de Physiologie de la Nutrition (INRA), Universite Paris-Sud, Orsay, 405, Fr.
SOURCE: Journal of Lipid Research (1997), 38(1), 86-100
CODEN: JLPRAW; ISSN: 0022-2275
PUBLISHER: Lipid Research, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To examine the effects of .beta.-cyclodextrin (BCD), a non-absorbable carbohydrate, on lipid metab., growing pigs were fed a 0.3% cholesterol-enriched diet for 4 wk or this diet contg. 5% or 10% BCD. Pigs fed a basal diet without added cholesterol or BCD were used as controls. The cholesterol-rich diet induced hypercholesterolemia (1.75 vs. 0.84 g/l plasma) due to increased LDL concn., delayed the plasma clearance of vitamin A, enhanced liver cholesterol storage, lowered the hepatic activities of LDL-receptors (by 47%) and HMG-CoA reductase (by 62%), stimulated cholesterol 7.alpha.-hydroxylase (.times.3), and accelerated the fecal output of neutral sterols (.times.4). Addn. of BCD to the cholesterol-rich diet prevented the elevation of plasma cholesterol due to dietary cholesterol excess. Moreover, BCD produced a dose-dependent effect in reducing liver cholesterol storage, stimulating hepatic cholesterogenesis, increasing the proportion of primary bile acids in bile and in feces, and the fecal loss of neutral sterols and bile acids. Pigs receiving 10% BCD thus differed markedly from controls, esp. for HMG-CoA reductase and cholesterol 7.alpha.-hydroxylase hepatic activities (.times.5), and fecal output of total bile acids (.times.3) and hyocholic acid (.times.20), and their overall cholesterol **synthesis** was higher (+50%), despite the abundant dietary cholesterol. Owing to the property of BCD to bind cholesterol and bile acids in vitro, these results suggest that this resistant carbohydrate accelerates body cholesterol turnover by reducing cholesterol absorption, increasing cholesterol and bile acid **synthesis**, and altering the action of the intestinal microflora.

L29 ANSWER 32 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 14
ACCESSION NUMBER: 1996:600912 HCAPLUS
DOCUMENT NUMBER: 125:241825
TITLE: The **protective** properties of carnosine and . **beta.-cyclodextrin** in photoreactions of **nucleic** acid bases
AUTHOR(S): Yakovlev, D. Yu.
CORPORATE SOURCE: Englehardt Institute Molecular Biology, Russian Academy Sciences, Moscow, 117984, Russia
SOURCE: Collection of Czechoslovak Chemical Communications (1996), 61(Spec. Issue), S142-S144
CODEN: CCCCAK; ISSN: 0010-0765
PUBLISHER: Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Carnosine and related compds. were tested for protection of thymine in photoredn. by the combined action of UV light and hypophosphite. Carnosine, homocarnosine and anserine were found to be the best protectors sufficiently preserving thymine photoconversion at 10 **mM** and practically fully suppressing the reaction at 50 **mM**. The action of compds. tested for thymine protection was as follows: anserine > homocarnosine > carnosine >> histidine = N-methylimidazole > histamine >>

imidazole. It was also shown that .beta.-**cyclodextrin** effectively **protects** thymine in TpT against the action of UV light and NaH2PO2.

L29 ANSWER 33 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 15
ACCESSION NUMBER: 1996:311119 BIOSIS
DOCUMENT NUMBER: PREV199699033475
TITLE: Analysis of **cyclodextrins** using a calorimetric biosensor.
AUTHOR(S): Kolb, Michael; Zentgraf, Brigitte (1); **Arvidsson, Peer**; Mattiasson, Bo; Danielsson, Bengt
CORPORATE SOURCE: (1) Technical Univ. Furtwangen, Dep. Chemical Engineering Biotechnol., Lab. Biochem., D-78054 Villingen-Schwennigen, Jakob-Kienzle-Strasse 17 Germany
SOURCE: Journal of Chemical Technology and Biotechnology, (1996) Vol. 66, No. 1, pp. 15-18.
ISSN: 0268-2575.
DOCUMENT TYPE: Article
LANGUAGE: English
AB A thermostable alpha-amylase catalyzed the exothermal hydrolysis of **cyclodextrins**. It was immobilized covalently via a spacer on controlled pore glass (CPG-10) or Silicagel. The temperature signal caused by the reaction heat of the **cyclodextrin** hydrolysis was determined in a one column calorimetric system (enzyme thermistor). It was correlated to the **cyclodextrin** concentration and depended on the type of enzyme carrier and kind of **cyclodextrin** hydrolyzed. The proposed technique offers a direct route to the determination of alpha-amylase activity, and the results are of importance for analysis of **cyclodextrin** concentration.

L29 ANSWER 34 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 16
ACCESSION NUMBER: 1996:362490 HCAPLUS
DOCUMENT NUMBER: 125:109214
TITLE: Biochemical analysis of **cyclodextrins** using an enzyme thermistor
AUTHOR(S): Kolb, M.; Zentgraf, B.; Mattiasson, B.; **Arvidsson, P.**; Danielsson, B.
CORPORATE SOURCE: Technical University of Furtwangen, Department of Chemical Engineering and Biotechnology, Laboratory of Biochemistry, Jakob-Kienzle-Strasse 17, D-78054 Villingen-Schwenningen, Germany
SOURCE: Thermochimica Acta (1996), 277, 1-6
CODEN: THACAS; ISSN: 0040-6031
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A thermostable .alpha.-amylase catalyzed the exothermal hydrolysis of **cyclodextrins**. It was immobilized covalently via a spacer on controlled pore glass (CPG-10) or Silicagel. The temp. signal caused by the reaction heat of the **cyclodextrin** hydrolysis was detd. in a one-column calorimetric system (enzyme thermistor). It was correlated to the **cyclodextrin** concn. and depended on the type of enzyme carrier and kind of **cyclodextrin** hydrolyzed. The proposed technique offers a direct route to the detn. of .alpha.-amylase activity, and the results are of importance for anal. of **cyclodextrin** concn.

L29 ANSWER 35 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 17

ACCESSION NUMBER: 1995:283669 HCAPLUS
DOCUMENT NUMBER: 122:91378
TITLE: Supported Monolayers Containing Preformed Binding Sites. **Synthesis** and Interfacial Binding Properties of a Thiolated .beta.-Cyclodextrin Derivative
AUTHOR(S): Rojas, Maria T.; Koeniger, Rainer; Stoddart, J. Fraser; Kaifer, Angel E.
CORPORATE SOURCE: Chemistry Department, University of Miami, Coral Gables, FL, 33124, USA
SOURCE: Journal of the American Chemical Society (1995), 117(1), 336-43
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Per-6-thio-.beta.-cyclodextrin (2) was prepd. in two steps from .beta.-cyclodextrin. Receptor 2 is a .beta.-cyclodextrin deriv. in which all the primary hydroxyl groups were replaced by thiol groups. As such, 2 chemisorbs onto gold surfaces forming at least six S-Au bonds per receptor mol. Although this derivatization process leads to imperfect monolayers in which a substantial fraction of the gold surface remains uncovered, the monolayer defects can be covered by treatment with a soln. of ferrocene and pentanethiol. Ferrocene, an excellent substrate for **.beta.-cyclodextrin, protects** the monolayer binding sites, directing the pentanethiol mols. to seal defective sites instead of the cyclodextrin cavities. Electrodes derivatized by this procedure showed effective binding properties when immersed in aq. solns. contg. low concns. (<60 .mu.M) of ferrocene. Their voltammetric response exhibited the waves anticipated for the reversible oxidn. of the surface-confined (cyclodextrin-bound) ferrocene mols. The process of interfacial ferrocene complexation has the expected dynamic character by competition expts. with m-toluic acid (mTA) in which the surface-confined voltammetric waves of ferrocene were gradually lost as increasing mTA concns. were added to the soln.

L29 ANSWER 36 OF 53 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95343104 EMBASE
DOCUMENT NUMBER: 1995343104
TITLE: 2-**Hydroxypropyl-.beta.-cyclodextrin** in the **protection** of haemolysis induced by bile acid.
AUTHOR: Vandelli M.A.; Panini R.; Salvioli G.; Bernabei M.T.; Cameroni R.
CORPORATE SOURCE: Dipartimento Scienze Farmaceutiche, Universita di Modena,Modena, Italy
SOURCE: Farmacevtski Vestnik, (1995) 46/SPEC. ISS. (275-276).
ISSN: 0014-8229 CODEN: FMVTAV
COUNTRY: Slovenia
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L29 ANSWER 37 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:326076 HCAPLUS
DOCUMENT NUMBER: 120:326076
TITLE: Selectively acetylation of cyclodextrins

Search completed by David Schreiber 308-4292

INVENTOR(S): Yoshinaga, Masanobu
PATENT ASSIGNEE(S): Toppan Printing Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 10 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 06009709	A2	19940118	JP 1992-218326	19920724
JP 2762859	B2	19980604		

PRIORITY APPLN. INFO.: JP 1992-137799 19920430

AB The title process is carried out by protection and deprotection of unacetylated OH groups in combination with ordinary acetylation of cyclodextrins. Anhydroglycosyl unit-based 2-, 3- or 6-monoacetylated, and 2,6- or 3,6-diacetylated cyclodextrins are prepd. in this manner. Tertiary-butyldimethylsilyl protective groups are prefered for protection of C-6 primary OH and OH groups of C-2 positions in early **synthetic** stage, while other popular groups such as benzyl, allyl and pyranyl groups can be used on other OH groups. Complete pathways of the **syntheses** are included.

L29 ANSWER 38 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1994:477700 HCAPLUS
DOCUMENT NUMBER: 121:77700
TITLE: Stabilizing effect of amphiphilic excipients on the freeze-thawing and freeze-drying of lactate dehydrogenase
AUTHOR(S): Izutsu, Ken-ichi; Yoshioka, Sumie; Terao, Tadao
CORPORATE SOURCE: Natl. Int. Health Sci., Tokyo, 158, Japan
SOURCE: Biotechnology and Bioengineering (1994), 43(11), 1102-7
CODEN: BIBIAU; ISSN: 0006-3592
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of amphiphilic excipients on the inactivation of lactate dehydrogenase (LDH) during freeze-thawing and freeze-drying were studied. Some amphiphilic excipients such as hydroxypropyl-.beta.-cyclodextrin (HP-.beta.-CD), CHAPS, polyethylene glycol (PEG) 3350, and a sucrose fatty acid monoester prevented LDH inactivation during freeze-thawing and freeze-drying at a lower concn. than sugars and amino acids. Polyoxyethylene 9 lauryl ether and PEG 400 protected LDH during freeze-thawing but not during freeze-drying. The buffer concn. of the soln. to be freeze-dried (10, 50, and 200 **mM**) affected the stabilizing effect of trehalose, but not that of HP-.beta.-CD.

L29 ANSWER 39 OF 53 MEDLINE DUPLICATE 18
ACCESSION NUMBER: 94300511 MEDLINE
DOCUMENT NUMBER: 94300511 PubMed ID: 8027925
TITLE: Effect of **hydroxypropyl-beta-cyclodextrin** on the antimicrobial action of **preservatives**.
AUTHOR: Lehner S J; Muller B W; Seydel J K
CORPORATE SOURCE: Department of Pharmaceutics and Biopharmaceutics, Christian Albrecht University, Kiel, Germany.
SOURCE: JOURNAL OF PHARMACY AND PHARMACOLOGY, (1994 Mar) 46 (3) 186-91.

Search completed by David Schreiber 308-4292

Journal code: 0376363. ISSN: 0022-3573.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199408
ENTRY DATE: Entered STN: 19940818
Last Updated on STN: 19940818
Entered Medline: 19940808

AB The interaction between **hydroxypropyl-beta-cyclodextrin** (HP-**beta**-CyD) and several **preservatives** with different chemical structures was investigated in aqueous solution. Complex stability constants of the 1:1 complexes were calculated from differential spectra. Using the serial dilution test the antimicrobial activities of the preservatives and their complexes against Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli and Candida albicans were tested and MIC values determined. For highly water-soluble substances like thimerosal and bronopol, low or no inactivation was found; the more lipophilic substances, such as the phenolic **compounds**, showed strong inactivation when used in combination with HP-beta-CyD. The loss in activity by complex formation correlated with the bound fraction, thus suggesting that the appropriate antimicrobial substance for the preservation of cyclodextrin solutions can be selected according to the results of this study.

L29 ANSWER 40 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 19
ACCESSION NUMBER: 1994:143920 HCAPLUS
DOCUMENT NUMBER: 120:143920
TITLE: Release characteristics of nifedipine from 2-**hydroxypropyl-.beta.-cyclodextrin** complex during **storage** and its modification of hybridizing polyvinylpyrrolidone K-30
AUTHOR(S): Wang, Zheng; Hirayama, Fumitoshi; Ikegami, Kengo; Uekama, Kaneto
CORPORATE SOURCE: Fac. Pharm. Sci., Kumamoto Univ., Kumamoto, 862, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1993), 41(10), 1822-6
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Amorphous nifedipine powders were prepd. by spray-drying with 2-hydroxypropyl-.beta.-cyclodextrin (HP-.beta.-CyD) or polyvinylpyrrolidone K-30 (PVP). Upon storage of the products at a high temp. and humidity, nifedipine crystd. in matrixes, yielding both bigger crystals (>50 .mu.m) in a PVP matrix and smaller crystals (about 5 .mu.m) in a HP-.beta.-CyD matrix. The release of nifedipine from tablets contg. the HP-.beta.-CyD complex was accelerated upon storage, whereas that from the PVP solid dispersion was decelerated. The deceleration of the release rate was attributable to the growth of nifedipine crystals with a larger size in the PVP matrix. The release of nifedipine from the HP-.beta.-CyD complex at the early period of storage, the inhibitory effect of HP-.beta.-CyD on the crystal growth of nifedipine took effect, leading to the release acceleration. To maintain the improved release of nifedipine over a long period of storage, a possible combination of HP-.beta.-CyD and PVP was investigated to act as a hybridizing drug carrier. Among various compns., the 1:3:1 (nifedipine/PVP/HP-.beta.-CyD, wt. ratio) product gave the most appropriate release profile without any decreased release of nifedipine at the early and late stages of storage.

L29 ANSWER 41 OF 53 MEDLINE
ACCESSION NUMBER: 94348813 MEDLINE
DOCUMENT NUMBER: 94348813 PubMed ID: 8069577
TITLE: Minimization of shaking-induced formation of insoluble aggregates of insulin by cyclodextrins.
AUTHOR: Banga A K; Mitra R
CORPORATE SOURCE: Department of Pharmacal Sciences, Auburn University, AL 36849.
SOURCE: JOURNAL OF DRUG TARGETING, (1993) 1 (4) 341-5.
Journal code: 9312476. ISSN: 1061-186X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199409
ENTRY DATE: Entered STN: 19941006
Last Updated on STN: 19941006
Entered Medline: 19940929

AB Aggregation is known to complicate insulin delivery and the processing and formulation of biotechnology-derived **peptide/protein** drugs. Shaking-induced formation of insoluble aggregates in bovine insulin and the potential role of cyclodextrins in preventing such aggregation were investigated. Insulin, dissolved in phosphate buffer, pH 7.2, and preserved with 2 mg/ml of phenol was aggregated, in triplicate, by shaking at 450 rpm for 2.5 days on a gyratory shaker. Visible aggregation was quantitated by measuring optical density in the visible range on a spectrophotometer. Solutions were then filtered through a 0.22 mu filter and the amount of insulin remaining in filtrate was determined by HPLC. Aggregation increased at lower concentrations, with solutions turning milky at 0.5 mg/ml; HPLC assay of filtrate indicated a complete loss of insulin. Under the same conditions, except for shaking, control solutions exhibited no insulin loss, excluding absorption as a cause of the insulin loss. The use of cyclodextrins (0.5 mg/ml) to stabilize insulin was investigated. alpha-, beta-, gamma- and hydroxypropyl-beta-cyclodextrin, each at 1.5% level, were used to prevent aggregation. The efficacy of cyclodextrins in preventing aggregation (% insulin aggregated in parentheses), was: **hydroxypropyl**-beta- (15) approximately **beta-** (18) > alpha- (54). No **protection** was observed with gamma-**cyclodextrin**.

L29 ANSWER 42 OF 53 EMBASE
ACCESSION NUMBER: 93241808 EMBASE
DOCUMENT NUMBER: 1993241808
TITLE: New polyfunctional derivatives of .beta.-cyclodextrin suited for the formulation of drug release systems.
AUTHOR: Solaro R.; D'Antone S.; Bemporad L.; Chiellini E.
CORPORATE SOURCE: Dept Chemistry/Industrial Chemistry, University of Pisa, via Risorgimento 35,56126 Pisa, Italy
SOURCE: Journal of Bioactive and Compatible Polymers, (1993) 8/3 (236-250).
ISSN: 0883-9115 CODEN: JBCPEV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 027 Biophysics, Bioengineering and Medical Instrumentation
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

Search completed by David Schreiber 308-4292

AB New functional derivatives of .beta.-cyclodextrin were obtained by grafting **.beta.-cyclodextrin** with epoxides of **protected** polyols, such as glycidylisopropylideneglycerol, glycidyldiisopropylidenexylitol and glycidyldiisopropylidenearabitol. The glycidyl ether of 2-pyrrolidone was also used. The reaction products have a degree of substitution per glucose residue included between 0.5 and 1. Selective removal of protecting groups from cyclodextrin substituents, carried out under conditions not affecting the integrity of the cyclodextrin ring, gave rise to hydrosoluble cyclodextrin derivatives whose hydrophilic/hydrophobic balance was modulated by controlling the extent of deprotection. The unusual solubility in water, greater than 350%, for both protected and deprotected derivatives, represents a breakthrough for a wide variety of applications requiring polymeric materials with remarkable water solubility.

L29 ANSWER 43 OF 53 SCISEARCH COPYRIGHT 2003 ISI (R)
ACCESSION NUMBER: 93:726311 SCISEARCH
THE GENUINE ARTICLE: MK006
TITLE: BETA-CYCLODEXTRIN TETRADECASULFATE TETRAHYDROCORTISOL PLUS-OR-MINUS MINOCYCLINE AS MODULATORS OF CANCER THERAPIES IN-VITRO AND IN-VIVO AGAINST PRIMARY AND METASTATIC LEWIS LUNG-CARCINOMA
AUTHOR: TEICHER B A (Reprint); SOTOMAYOR E A; HUANG Z D; ARA G; HOLDEN S; KHANDEKAR V; CHEN Y N
CORPORATE SOURCE: HARVARD UNIV, SCH MED, DANA FARBER CANC INST, 44 BINNEY ST, BOSTON, MA, 02115 (Reprint); JOINT CTR RADIAT THERAPY, BOSTON, MA, 02115
COUNTRY OF AUTHOR: USA
SOURCE: CANCER CHEMOTHERAPY AND PHARMACOLOGY, (DEC 1993) Vol. 33, No. 3, pp. 229-238.
ISSN: 0344-5704.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: ENGLISH
REFERENCE COUNT: 74

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Tetrahydrocortisol, beta-cyclodextrin tetradecasulfate, and minocycline used alone or in combination are not very cytotoxic toward EMT-6 mouse mammary tumor cells growing in monolayer. Tetrahydrocortisol (100 muM, 24 h) and **beta-cyclodextrin** tetradecasulfate (100 muM, 24 h) **protected** EMT-6 cells from the cytotoxicity of CDDP, melphalan, 4-hydroperoxycyclophosphamide, BCNU, and X-rays under various conditions of oxygenation and pH. Minocycline (100 muM, 24 h) either had no effect upon or was additive with the antitumor alkylating agents or X-rays in cytotoxic activity toward the EMT-6 cells in culture. The combination of the three modulators either had no effect upon or was to a small degree protective against the cytotoxicity of the antitumor alkylating agents or X-rays. The Lewis lung carcinoma was chosen for primary tumor growth-delay studies and tumor lung-metastases studies. Tetrahydrocortisol and beta-cyclodextrin tetradecasulfate were given in a 1:1 molar ratio by continuous infusion over 14 days, and minocycline was given i.p. over 14 days, from day 4 to day 18 post tumor implantation. The combination of tetrahydrocortisol/beta-cyclodextrin tetradecasulfate diminished the tumor growth delay induced by CDDP and melphalan and produced modest increases in the tumor growth delay produced by cyclophosphamide and radiation. Minocycline co-treatment increased the tumor growth delay produced by CDDP, melphalan, radiation, bleomycin, and, especially cyclophosphamide, where 4 of 12 animals receiving minocycline (14 x 5 mg/kg, days 4-18) and cyclophosphamide (3 x 150 mg/kg, days 7, 9,

11) were long-term survivors. The 3 modulators given in combination produced further increases in tumor growth delay with all of the cytotoxic therapies, and 5 of 12 of the animals treated with the 3-modulator combination and cyclophosphamide were long-term survivors. Although neither tetrahydrocortisol/beta-cyclodextrin tetradecasulfate, minocycline, nor the three modulator combination impacted the number of lung metastases, there was a decrease in the number of large lung metastases. Treatment with the cytotoxic therapies alone reduced the number of lung metastases. Addition of the modulators to treatment with the cytotoxic therapies resulted in a further reduction in the number of lung metastases. These results indicate that agents that inhibit the breakdown of the extracellular matrix can be useful additions to the treatment of solid tumors.

L29 ANSWER 44 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.DUPLICATE 20
ACCESSION NUMBER: 1993:297544 BIOSIS
DOCUMENT NUMBER: PREV199396015769
TITLE: Stabilization of beta-galactosidase by amphiphilic additives during freeze-drying.
AUTHOR(S): Izutsu, Ken-Ichi (1); Yoshioka, Sumie; Terao, Tadao
CORPORATE SOURCE: (1) Natl. Inst. Hyg. Sci., 1-18-1 Kamiyoga, Setagaya-ku, Tokyo 158 Japan
SOURCE: International Journal of Pharmaceutics (Amsterdam), (1993) Vol. 90, No. 3, pp. 187-194.
ISSN: 0378-5173.
DOCUMENT TYPE: Article
LANGUAGE: English
AB The effects of amphiphilic additives on inactivation of beta-galactosidase during freeze-drying were studied in comparison with those of sugars and amino acids. The activity loss was greater when the enzyme was freeze-dried from solutions of lower enzyme concentration without additives. Well-known cryoprotectants such as sugars and amino acids provided concentration-dependent **preservation** of enzyme activity. **Hydroxypropyl-beta-cyclodextrin** (HP-**beta**-CD), 2,6-di-O-methyl-beta-cyclodextrin (DM-beta-CD), 3-((3-cholamidopropyl)dimethylammonio)-1-propanesulfonate (CHAPS) and sucrose fatty acid monoester stabilized the enzyme at much lower concentrations than-sugars and amino acids. Polyethylene glycol 400 (PEG 400), polyoxyethylene 9 lauryl ether (polydocanol) and sodium dodecyl sulfate (SDS), however, were ineffective or rather induced inactivation. High-performance size-exclusion chromatography indicated the formation of soluble aggregates during freeze-drying without additives, which was inhibited by the sugar ester. SDS-PAGE indicated that the aggregates were formed by noncovalent bonding.

L29 ANSWER 45 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1992:257758 HCAPLUS
DOCUMENT NUMBER: 116:257758
TITLE: Manufacture of cyclodextrin-immobolized polymers
INVENTOR(S): Yoshinaga, Masanobu
PATENT ASSIGNEE(S): Toppan Printing Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 04025504	A2	19920129	JP 1990-130513	19900521

PRIORITY APPLN. INFO.: JP 1990-130513 19900521

AB The title products are obtained by (a) blocking 1 methylol group of the cyclodextrin substrate (I) with trityl chloride, (b) esterifying or etherifying the protected I, (c) deprotecting giving monohydroxyl-I, (d) allowing to react with .alpha.,.beta.-unsatd. acid halides to give addn.-polymerizable monomers, and (e) polymg. the monomers.

L29 ANSWER 46 OF 53 HCAPLUS COPYRIGHT 2003 ACS DUPLICATE 21
ACCESSION NUMBER: 1992:476388 HCAPLUS
DOCUMENT NUMBER: 117:76388
TITLE: Interactions between **preservatives** and 2-**hydroxypropyl .beta.-cyclodextrin**
AUTHOR(S): Loftsson, T.; Stefansdottir, O.; Fridriksdottir, H.; Guomundsson, O.
CORPORATE SOURCE: Dep. Pharm., Univ. Iceland, Reykjavik, IS-101, Iceland
SOURCE: Drug Development and Industrial Pharmacy (1992), 18(13), 1477-84
CODEN: DDIPD8; ISSN: 0363-9045
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interactions between several commonly used preservatives, i.e. benzalkonium chloride, chlorhexidine gluconate, chlorobutanol, methylparaben and propylparaben, and 2-hydroxypropyl .beta.-cyclodextrin were investigated. The interactions were 2-fold. Firstly, the preservative mols. displace the drug mols. from the cyclodextrin cavity, thus, reducing the solubilizing effects of the cyclodextrin. Secondly, the antimicrobial activity of the preservatives were reduced by formation of preservative-cyclodextrin inclusion complexes. The magnitude of the interactions were dependent on the degree of complexation.

L29 ANSWER 47 OF 53 MEDLINE DUPLICATE 22
ACCESSION NUMBER: 92333423 MEDLINE
DOCUMENT NUMBER: 92333423 PubMed ID: 1352820
TITLE: Inhibitory effect of 2-hydroxypropyl-beta-cyclodextrin on crystal-growth of nifedipine during storage: superior dissolution and oral bioavailability compared with polyvinylpyrrolidone K-30.
AUTHOR: Uekama K; Ikegami K; Wang Z; Horiuchi Y; Hirayama F
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Kumamoto University, Japan.
SOURCE: JOURNAL OF PHARMACY AND PHARMACOLOGY, (1992 Feb) 44 (2) 73-8.
Journal code: 0376363. ISSN: 0022-3573.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199208
ENTRY DATE: Entered STN: 19920904
Last Updated on STN: 19950206
Entered Medline: 19920819

AB To prevent the crystal-growth of nifedipine during **storage**, 2-**hydroxypropyl-beta-cyclodextrin** (HP-**beta**-CyD) was employed as a hydrophilic drug carrier and compared with polyvinylpyrrolidone K-30 (PVP). Amorphous nifedipine powders were

prepared by spray-drying with HP-beta-CyD or PVP, and their crystal-growing behaviour at accelerated storage conditions were examined by X-ray diffraction analysis and microscopy. Although PVP initially retarded the crystallization of nifedipine, it failed to control the increase of crystal size after prolonged storage at 60 degrees C, 75% r.h., resulting in a remarkable decrease in dissolution rate in water. In sharp contrast, a relatively fine and uniform size of nifedipine crystals was maintained in the HP-beta-CyD system even after accelerated storage conditions. The enhanced dissolution observed for all the HP-beta-CyD systems in a dissolution medium containing 0.1% non-ionic surfactant HCO-60 were clearly reflected in the in-vivo absorption of nifedipine following oral administration to dogs. These results suggest that HP-beta-CyD is particularly useful in solving problems encountered on storage of amorphous nifedipine in solid dosage forms.

L29 ANSWER 48 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1992:39555 BIOSIS
DOCUMENT NUMBER: BR42:15705
TITLE: INFLUENCE OF LYOPHILIZATION ON THE STABILITY OF A MOUSE IGG2A MONOCLONAL ANTIBODY MN12.
AUTHOR(S): RESSING M E; JISKOOT W; TALSMA H; BEUVERY E C; CROMMELIN D J A
CORPORATE SOURCE: LABORATORY INACTIVATED VIRAL VACCINES, NATIONAL INSTITUTE PUBLIC HEALTH ENVIRONMENTAL PROTECTION, BILTHOVEN, NETH.
SOURCE: AAPS (AMERICAN ASSOCIATION OF PHARMACEUTICAL SCIENTISTS) SIXTH ANNUAL MEETING AND EXPOSITION, WASHINGTON, D.C., USA, NOVEMBER 17-21, 1991. PHARM RES (N Y), (1991) 8 (10 SUPPL), S52.
CODEN: PHREEB. ISSN: 0724-8741.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English

L29 ANSWER 49 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:536329 HCAPLUS
DOCUMENT NUMBER: 111:136329
TITLE: Alkali **compounds** for preserving etherified cyclodextrin aqueous solutions
INVENTOR(S): Kamya, Hiroshi; Sawada, Hiroki; Ito, Susumu; Kobayashi, Tooru
PATENT ASSIGNEE(S): Kao Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01110503	A2	19890427	JP 1987-267483	19871022
JP 2651580	B2	19970910		

PRIORITY APPLN. INFO.: JP 1987-267483 19871022

AB Preserving etherified cyclodextrin aq. solns. against spoiling is done by addn. of alkali compds. to increase the pH to 12.0 or above. A 20% aq. soln. of Me .beta.-cyclodextrin was mixed with 0.05% NaOH to adjust the pH to 12.1 showing no spoiling after 28 days, vs. spoiling if the NaOH was added at 0.01% (pH 10.9).

Search completed by David Schreiber 308-4292

L29 ANSWER 50 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1989:626859 HCAPLUS
DOCUMENT NUMBER: 111:226859
TITLE: **Design** and production of **peptides** mimicking the active site of serine esterases with covalent binding to the organophosphorus poison soman
AUTHOR(S): Seltzman, H. H.
CORPORATE SOURCE: Research Triangle Inst., Research Triangle Park, NC, USA
SOURCE: Report (1988), Order No. AD-A204765, 133 pp. Avail.: NTIS
From: Gov. Rep. Announce. Index (U. S.) 1989, 89(13), Abstr. No. 935,761
DOCUMENT TYPE: Report
LANGUAGE: English
AB The objective of this research program was to **design**, **synthesize** and test mimics of acetylcholinesterase (AChE), the natural target of soman, that would scavenge the organophosphate poison soman in vivo and thereby provide protection against this chem. warfare agent. During this program, compds. were developed that were active in vivo, affording protection to AChE, and active in vivo, affording protection against lethality in vivo, affording protection against lethality to guinea pigs. The naturally occurring .beta.-cyclodextrin (.beta.-CD) scavenged soman in vitro at 0.001M, thus affording protection to AChE; covalent bonding was demonstrated by no reversibility of scavenging and by the isolation of .beta.-CD soman adducts. Functional modifications introduced on the narrow primary rim of .beta.-CD were generally without effect in improving activity. Substituents introduced on the more open, secondary rim of .beta.-CD resulted in diminished activity. Dramatic improvement in scavenging was achieved with a .beta.-CD that was rigidly capped on the primary rim. The most active compd. tested in vitro was also active in vivo, affording a protection ratio of greater than 1.5 in guinea pigs at a 20 mg dose. Higher dosing to afford protection against multiple LD50's should be possible for this compd. because of the low toxicity of cyclodextrins.

L29 ANSWER 51 OF 53 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1990:117481 HCAPLUS
DOCUMENT NUMBER: 112:117481
TITLE: Long-term **storage** stability studies on flavor-**.beta.-cyclodextrin** complexes
AUTHOR(S): Szente, L.; Harangi, J.; Szejtli, J.
CORPORATE SOURCE: Cyclodextrin Lab., Chinoin Pharm.-Chem. Works, Budapest, Hung.
SOURCE: Proc. Int. Symp. Cyclodextrins, 4th (1988), 545-9. Editor(s): Huber, O.; Szejtli, Jozsef. Kluwer: Dordrecht, Neth.
CODEN: 56SBAU
DOCUMENT TYPE: Conference
LANGUAGE: English
AB .beta.-Cyclodextrin inclusions of natural and **synthetic** flavors and flavoring substances were stored under normal conditions for 10 yr and their actual flavor contents were monitored. Comparative TLC and GC studies proved that mol. encapsulation of essential oils provided marked stability in long-term storage at ambient temp. and normal humidity. Flavors consisting of phenolic components were less resistant to long-term storage, and both the total flavor loss and the degree of deterioration of the retained flavor were greater than in the case of terpenoid and

phenylpropanoid inclusion complexes.

L29 ANSWER 52 OF 53 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1979:204332 BIOSIS
DOCUMENT NUMBER: BA68:6836
TITLE: SPECIFIC INCLUSION CATALYSIS BY BETA CYCLO DEXTRIN IN THE 1 STEP PREPARATION OF VITAMIN K-1 OR VITAMIN K-2 ANALOGS.
AUTHOR(S): TABUSHI I; YAMAMURA K; FUJITA K; KAWAKUBO H
CORPORATE SOURCE: DEP. SYNTH. CHEM., KYOTO UNIV., YOSHIDA, KYOTO 606, JPN.
SOURCE: J AM CHEM SOC, (1979) 101 (4), 1019-1026.
CODEN: JACSAT. ISSN: 0002-7863.
FILE SEGMENT: BA; OLD
LANGUAGE: English

AB Electrophilic allylation at the C3 position of 2-methylhydroaphthoquinone-1,4 (5) with allyl, crotyl, methallyl, or prenyl bromide was successfully developed to give a highly selective 1-step preparation of the corresponding vitamin K1 (or K2) analogs by the use of .beta.-cyclodextrin in dilute aqueous alkaline solution. In order to elucidate the basis of this interesting inclusion catalysis which resembles ligase and/or oxidase reactions, mechanistic studies were carried out. The specific inclusion binding of the substrate 5 by .beta.-cyclodextrin (Ka = 490 M-1, pH 3.55) facilitated the proton dissociation of 5, resulting in a decrease in its pKa value from 9.45 for uncomplexed 5 to 8.9 for complexed 5. Based on kinetic results showing that the rate of allylation of .alpha.-naphthol at pH 10.4 was enhanced by 2.5 to 3.5 times in the presence of .beta.-cyclodextrin, it was concluded that the nucleophilic reactivity of the partially charged carbanion increased in the hydrophobic cavity and, therefore, the allylation reactions were accelerated by .beta.-cyclodextrin. Another noteworthy aspect of the mechanism was seen in the interesting observation that the 2-methylnaphthosemiquinone anion radical (detected by ESR) which was produced by oxidation of the allylated hydronaphthoquinone by molecular O2 was strongly bound by .beta.-cyclodextrin. This indicated either the possibility that the oxidation proceeds predominantly through the complexed form of the allylated hydroquinone or that the lifetime of the semiquinone anion radical is prolonged by the inclusion binding. Vitamin K analogues allylated naphthoquinone and 2-methylnaphthoquinone-1,4, which were products, were highly susceptible to oxidative **degradation** due to the attack of H2O2, which was another product of the oxidation step. . **beta.-Cyclodextrin** effectively **protected** those quiniones from the attack by H2O2, and their oxidation rates were from 1/9 to 1/17 of that for the uncomplexed quinone.

L29 ANSWER 53 OF 53 MEDLINE DUPLICATE 23
ACCESSION NUMBER: 76069315 MEDLINE
DOCUMENT NUMBER: 76069315 PubMed ID: 127797
TITLE: Studies on the fatty acid inactivation of phosphofructokinase.
AUTHOR: Ramadoss C S; Uyeda K; Johnston J M
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1976 Jan 10) 251 (1) 98-107.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197603
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19970203

Search completed by David Schreiber 308-4292

Entered Medline: 19760301

AB Investigation of phosphofructokinase in normal and regenerating livers led to the discovery of an inactivating factor in the extracts of these livers. The inactivating factor was found to be a **mixture** of free fatty acids. The fatty acid compositions of the normal and regenerating livers are the same, but the concentrations of most of the fatty acids are at least 3 to 4 times higher in the latter. Inactivation of phosphofructokinase by palmitate and oleate was investigated using purified rabbit muscle enzyme. Incubation of the enzyme with palmitate (250 muM) or oleate (50 muM) resulted in rapid inactivation of the enzyme with biphasic curves. The concentrations of oleate and palmitate required to produce 50% inactivation of the enzyme were 35 muM and 75 muM, respectively. Fructose-6-P (0.5 **mM**), MgATP, (1 **mM**), fructose-1,6-P2 (1 **mM**), AMP (1 **mM**), and cyclic adenosine 3':5'-monophosphate (20 muM) protected the enzyme against inactivation when these metabolites were incubated with the enzyme before the addition of fatty acid. Bovine serum albumin (100 muM) and **beta-cyclodextrin** (0.25 **mM**) also **protected** the enzyme against the inactivation. However, if the enzyme was inactivated by fatty acid, subsequent addition of the above metabolites or bovine serum albumin did not reactivate the enzyme. Binding studies with [3H]oleate revealed at least three types of binding sites. The first site binds 2 to 4 mol of oleate/mol of enzyme. Oleate binding to this site did not seem to affect the enzyme activity. The second binding site binds 5 to 15 mol of oleate/mol of enzyme resulting in complete loss of the activity. This is followed by an increase in oleate binding to the third site of the enzyme. Sucrose density gradient centrifugation of oleate-inactivated enzyme indicated that the enzyme dissociated to the dimeric form. Similarly, centrifugation of [3H]oleate-treated enzyme revealed that all polymeric forms of phosphofructokinase bound approximately 6 to 8 mol of oleate/mol of enzyme. In the presence of fructose-6-P, oleate is bound to the polymers to a lesser degree and therefore protects against the fatty acid inactivation. Various polymers which are cross-linked with dimethylsuberimidate are also inhibited by oleate.